Salvage Combination Chemotherapy with Docetaxel, Ifosfamide and Cisplatin (DIP): Successful Treatment of a Case with Metastatic Testicular Immature Teratoma

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We present a case of metastatic testicular immature teratoma that was successfully treated despite resistance to standard chemotherapy and unsuccessful salvage surgery. At first, BEP (bleomycin, etoposide and cisplatin) treatment was performed but failed. The patient underwent incomplete retroperitoneal lymph node dissection. He was then referred to us. By the time of the referral lung and mediastinal lymph node metastasis had appeared and para-aortic lymph node metastasis had grown larger. We administered the DIP (docetaxel, ifosfamide and cisplatin) regimen as a second line chemotherapy, which was effective with 82% reduction of para-aortic lymph nodes, 88% of mediastinal lymph nodes and 85% of lung metastasis. We performed para-aortic lymph node dissection followed by resection of lung metastasis and mediastinal lymph node dissection. The patient is now followed-up at the outpatient clinic without evidence of recurrent disease 3.5 years after the last surgery.

Key words: testicular cancer – immature teratoma – chemotherapy – DIP

INTRODUCTION

There are only limited and incomplete data available on the treatment of chemorefractory testicular immature teratoma, probably because immature teratoma itself is encountered quite infrequently in testicular germ cell tumours (1). Even in the ovarian immature teratoma, which is the third most common germ cell neoplasm representing about 20% of the cases (2,3), little is known about the treatment of chemorefractory cases (4). DIP is a newly developed regimen which was demonstrated to be effective for urothelial carcinoma (5). As a pilot study we are investigating its clinical efficacy for metastatic testicular cancer. Here, we report successful treatment of metastatic testicular immature teratoma with combination chemotherapy with DIP after treatment failure of the prior standard chemotherapy and surgery.

CASE REPORT

A 38-year-old male noticed left testicular swelling in July, 2002, and as it became larger, he consulted an urologist on March 2003. He was diagnosed with testicular cancer with para-aortic lymph node metastasis. His serum alphafetoprotein and beta hCG values were normal. High orchiectomy followed by BEP (cisplatin 20 mg/m² for 5 days, etoposide 100 mg/m² for 5 days and bleomycin 30 units for 3 days) was performed. Despite the chemotherapy the para-aortic lymph nodes grew larger, so retroperitoneal lymph node dissection was performed. However, it was told that the dissection was incomplete because of some technical problems. Histologically the lymph node metastasis was immature teratoma with medulloblastomatous and rhabdomyoblastic components (Fig. 1A and B).

Local recurrence was detected of para-aortic lymph node metastasis and, additionally, mediastinal lymph node and left lung metastasis appeared. He was referred to us in October 2003.

As a second-line chemotherapy, according to our clinical protocol, we performed four cycles of DIP regimen (docetaxel 120 mg for 1 day, ifosfamide 2 g for 5 days and cisplatin 200 mg for 1 day) (5).

After the chemotherapy the para-aortic lymph nodes were reduced by 82%, mediastinal lymph nodes by 88% and lung metastasis by 85% (Figs 3 and 4), without major adverse effects except grade 4 granulocytopenia. We performed retroperitoneal lymph node dissection in March 2004, and...
performed mediastinal lymph node dissection and pulmonary right middle lobectomy in June 2004.

Histological examination revealed that these lymph nodes and the lung metastasis consisted of mature teratoma components and did not contain immature components.

Additional chemotherapy was not performed.

The patient is now followed-up at the outpatient clinic without evidence of recurrent disease 3.5 years after the last surgery.

DISCUSSION

For metastatic non-seminomatous germ cell testicular cases, neo-adjuvant chemotherapy followed by surgical resection is a standard treatment (1). In this case BEP administration was used as a first line chemotherapy. BEP is widely used for treatment of testicular germ cell tumors (1). BEP is also indicated as a standard adjuvant therapy for ovarian immature teratoma (3). However, only a few reports have been published on the treatment of chemorefractory cases of testicular or ovarian immature teratoma; salvage surgery seems effective (4).

Because the tumour in this case had shown resistance to BEP, we performed DIP as an alternative therapy. DIP is a newly developed regimen that has been shown effective for urothelial carcinoma with low toxicity (5). In that report, 14 cases of metastatic urothelial carcinoma were treated with this regimen, and 72% of them achieved partial response with durations ranging from 3 to 12 months. The major adverse effects were haematological, including granulocytopenia and thrombocytopenia. In our department, as a pilot study, we have administered the DIP regimen in cases of testicular cancer as a second-line chemotherapy, which was approved by the ethical committee in our hospital.

In this case DIP was indicated simply because it was a second-line chemotherapy in our department. However, retrospectively, the DIP might have been just the correct and rational regimen in this case; first because the drugs used in DIP are quite different from those in BEP, except cisplatin; secondly because ifosfamide and/or cisplatin in DIP have been shown to be effective and are widely used for non-epithelial malignant tumours including soft tissue

**Figure 1.** Histologically the dissected lymph node was diagnosed as immature teratoma at the initial hospital. In addition to the mature tissue, immature components included medulloblastomatous components.

**Figure 2.** Histologically the dissected lymph node was diagnosed as immature teratoma at the initial hospital. In addition to the mature tissue, immature components included rhabdomyocyte-like cells.

**Figure 3.** Abdominal CT demonstrated that the para-aortic lymph nodes, located behind the inferior vena cava (shown by arrow heads), were reduced by 88% after DIP. (A) Before chemotherapy. (B) After chemotherapy.

**Figure 4.** Chest CT also showed that lung metastasis (shown by arrow heads) was markedly reduced after DIP by 88%. (A) Before chemotherapy. (B) After chemotherapy.
sarcomas and brain tumours (6), as in our case the immature teratoma had medulloblastomatous and rhabdomyoblastic components; thirdly because docetaxel, which is a recently developed anti-tumour agent, is also reportedly effective in some kinds of sarcomas (7); and, finally, because docetaxel is not thought to evoke cross-resistance with cisplatin (8).

In this case, although it remains to be seen whether DIP or salvage surgery was essential for treatment, it was obvious that the tumour was rapidly and dramatically reduced after the DIP treatment. Considering that there are only a few regimens that are effective for immature teratoma, DIP may be a preferred regimen and could be useful and widely used as a second-line chemotherapy for immature teratoma.

Conflict of interest statement
None declared.

References